

Rejection under 35 U.S. C. § 103

1. Claims 1-10, 16-22 and 38

The Examiner maintained the rejection of claims 1-10, 16-22 and 38 as allegedly obvious over Ohnuki *et al.* (“Ohnuki”) in view of Garcia *et al.* (“Garcia”) and Chang *et al.* (“Chang”). The Examiner rejected applicants’ arguments because she alleges that the claims are not commensurate in scope with the arguments made in the March 22, 2002 response. However, applicants submit that the arguments presented regarding the PC-3 cell lines were made to show that Ohnuki does not disclose cells that possess the “metastatic potential” as defined in the specification in the paragraph bridging pages 4 and 5 and the first complete paragraph on page 5.

But more importantly, applicants submit that Ohnuki does not teach the claimed cell type and nor does Ohnuki render the claimed cell type obvious. Rather Ohnuki teaches disseminated human prostatic adenocarcinoma tumor cell lines that are autologous cells with metastatic potential that are derived from bone marrow. The language of claim 1 of the present invention is directed to “[a]n immortalized, non-small cell lung cancer, epithelial tumor cell...” This latter term has an art-recognized meaning and does not encompass the cells disclosed in Ohnuki. For example, the Online Dictionary of Cancer Terms provided by the National Cancer Institute provides a definition for “non-small cell lung cancer” as a group of lung cancers that includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. These cancers are lung cancers not prostatic.

Additionally, applicants provide scientific publications to further support their position that non-small cell lung cancers (NSCLC) is an art-recognized term that defines a particular type of cell. For example, Gazdar shows on page 261 that clinicians have broadly categorized bronchogenic cancers into two groups reflecting their biology and management; i.e., small cell lung cancers (SCLC) and non-small cell lung cancers (NSCLC). This publication looked at a number of different parameters of these two different classifications of lung cancers and compared them. Additionally, Riquet *et al.* provides the results of a study of non-small cell lung cancer and nodal disease patients. There two publications show that NSCLC is an art-recognized term that defines a specific type of lung cancer cell, and cannot be interpreted as any type of lung cancer cell that is not a small cell type. Applicants submit that the Examiner has improperly interpreted this term in claim 1, and assert that this term should be given its art-recognized meaning as

supported by the attached publications, which were invited by the Examiner. In regard to the interpretation of this term, the Examiner is urged to reconsider her position based upon the submitted information.

Applicants again respectfully traverse this rejection because the Examiner has used applicants' own disclosure and impermissible hindsight to combine Ohnuki, Garcia and Chang to arrive at the claimed invention.

The present invention provides immortalized non-SCLC epithelial tumor cells that are derived from the earliest metastasizing cells which have conserved the phenotype of the residual tumor cells present in the patient. See the paragraph bridging pages 4 and 5 of the specification. It is important to recognize these cells at this very early stage and generate quantities of them to analyze the early stages of cancer for identification and therapeutic methods. These epithelial tumor cells with metastatic potential have a clearly different expression pattern of surface markers as compared to primary tumor cells. The Examiner is referred to page 2, last four lines of the specification. Accordingly, the cells of the present invention are clearly distinct from primary tumor cells described in Ohnuki, which are human prostatic adenocarcinoma cells. Therefore, the skilled artisan would not have combined the Ohnuki disclosure with Garcia and Chang to arrive at the claimed immortalized non-SCLC epithelial tumor cells which express an immortalizing oncogene.

As argued on page 3 of the previous response, Ohnuki clearly teaches away from the claimed invention because the metastatic cell lines disclosed by Ohnuki are obtained from a patient suffering from undifferentiated Grade IV adenocarcinoma of the prostate metastatic to bone, as shown on page 524 of Ohnuki, right hand column, first paragraph of the "Materials and Methods" section. These cells cannot be characterized as being derived from the earliest metastasizing cells, as it is the case for the cells of the present invention.

Accordingly, the Examiner has failed to provide any prior art that discloses a non-small cell lung cancer cell, which is a specific type of cell. The cells described in Ohnuki are distinct from the cells of the present invention, and a person skilled in the art at the priority date of the present invention would not have been motivated to combine the teachings of Ohnuki with Garcia and Chang to arrive at the presently claimed cells.

The Examiner has cited Chang in combination with Ohnuki and Garcia but all that Chang provides are basic protocols for SV40 infections. Again, this reference as argued on

pages 4 and 5 of the previous response does not provide for an immortalized, non-small cell lung cancer epithelial tumor cell or a method to generate such a cell.

In addition to the above arguments, applicants believe that the obviousness rejection based on Ohnuki in view of Garcia and Chang is improper. As argued on page 5 of the previous response, Garcia does not disclose the transformation of a tumor cell but rather Garcia describes the transformation of a normal epithelial cell, and therefore the immortalization of a non-tumor cell. Therefore, Garcia teaches that tumorigenic cells can be obtained from normal epithelial cells by co-injecting SV40 and the human oncogene c-Ha-ras. Further, there is simply no motivation to utilize the method of Garcia to make metastatic cell lines of Ohnuki's cells.

Applicants respectfully disagree with the Examiner's rationale for combining the cited prior art and for utilizing impermissible hindsight to construct the present rejection based upon Applicants' own disclosure. It is applicants' position that the combination of the prior art fails to provide a suggestion to make the present invention. For all of the reasons and all of the arguments presented above, this rejection should be withdrawn.

2. Claims 1-12, 16-22, 31 and 38

Claims 1-12, 16-22, 31 and 38 are alleged to be obvious over Ohnuki *et al.* ("Ohnuki") in view of Garcia *et al.* ("Garcia"), Blankenstein *et al.* ("Blankenstein") and Chang *et al.* ("Chang"). The Examiner applies Ohnuki, Garcia and Chang as above and Blankenstein to teach the transfer of single cytokine genes into cancer cells. The addition of Blankenstein fails to cure the deficiencies in the primary references, and in view of the above arguments directed to the combination of the primary references, it is requested that this rejection be withdrawn.

3. Claims 1-10, 16-22, 31 and 38

Claims 1-10, 16-22, 31 and 38 are alleged to be obvious over Ohnuki *et al.* ("Ohnuki") in view of Garcia *et al.* ("Garcia"), Chang *et al.* ("Chang") and the Sigma Cell Culture Catalogue and Price List ("Sigma"). The Examiner applies Ohnuki, Garcia and Chang as above, and Sigma to teach to availability of growth factor supplements for use in the culture medium. The addition of Sigma fails to cure the deficiencies in the primary references, and in view of the all of the above arguments directed to the combination of the primary references, it is requested that this rejection be withdrawn.

4. Claims 1-10, 16-22, 33, 34 and 38

Claims 1-10, 16-22, 33, 34 and 38 are alleged to be obvious over Ohnuki *et al.* ("Ohnuki") in view of Garcia *et al.* ("Garcia"), Chang *et al.* ("Chang") and Gottlinger *et al.* ("Gottlinger"). The Examiner applies Ohnuki, Garcia and Chang, as above and Gottlinger to teach to epithelial surface antigens and adjuvants suitable for mounting an immunological response. The addition of Gottlinger fails to cure the deficiencies in the primary references, and in view of the all of the above arguments, it is requested that this rejection be withdrawn.

CONCLUSION

Applicants kindly request consideration of the arguments presented herein and the attached publications that were invited by the Examiner to provide support for the fact that the term "non-small cell lung cancer ... cell" has a specific art-recognized meaning. Applicants submit that this application is in condition for allowance, and they solicit an early indication to that effect. Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, a telephone call to the undersigned, at the telephone number listed below, is courteously invited.

Respectfully submitted,

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Date

FOLEY & LARDNER
3000 K Street, N.W.
Suite 500
Washington, D. C. 20007-5109
(202) 672-5300

Ruband C Post 35,792
Jayme A. Huleatt
Reg. No. 34,485